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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/039,171	01/03/2002	Robert Haley	UTSD:749US	7156

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EXAMINER	
WHITEMAN, BRIAN A	
ART UNIT	**PAPER NUMBER**
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/039,171	HALEY ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,9-25 and 36-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,9-16,19-25,36-43* is/are rejected.

7)☒ Claim(s) *17 and 18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

The election/restriction is moot in view of the cancellation of claims directed to non-elected inventions and as stated in the previous office action, claims 2 and 22 are rejoined with elected invention and examined.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 10-13, 19-25, 37-39 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Radtke (US 6,521,226) taken with Li et al. (Toxicology Letter 76:219-226, 1995, cited on an IDS) and Davies et al. (Nature Genetics 14:334-336, 1996, cited on an IDS). Radtke teaches that paraoxonase-1 (PON-1), when expressed has hydrolase activity for organophosphate. See columns 1 and 15-16. Radtke teaches that PON1 type R and Q are known variants in humans (columns 4-5 and 15-16). Radtke teaches using PON 1 in gene therapy using a number of viral vectors comprising and methods of delivery are known in the prior art (column 8-9). PON1 type Q phenotype has been correlated with higher paraoxonase activity than the type R phenotype (column 8). Radtke teaches using several routes of administration (including intravenous) to deliver the composition to a subject (column 6). An assay can be used to measure either phenotype or the ratio of the two phenotypes present in an individual (column 8). However, Radtke does not specifically teach identifying a subject at risk or exposed to an organophosphate toxin and administering an expression cassette comprising a nucleic acid encoding PON1 to the subject.

However, at the time the invention was made, Li et al. teach that paraoxonase protects animals against an organophosphate toxin (page 219). Li further teaches identifying animals that have been exposed to an organophosphate toxin (pages 220-221). Li teaches intravenous (i.v.) administration of PON to a mice exposed to an organophosphate toxin (page 221).

In addition, at the time the invention was made, for three decades it has been established that the main determinant of susceptibility to organophosphate poisoning is the activity level of PON 1 isoenzymes, and this relationship has been shown to hold across many species including humans. Davies teaches, "interspecies differences in PON1 activity correlate well with observed median lethal dose (LDs0) values [of organophophates]." See abstract.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Radtke taken with Li and Davies, namely to identify an animal exposed to an organophosphate toxin and express PON 1 in a cell or subject exposed to the organophosphate toxin. One of ordinary skill in the art would have been motivated to combine the teaching to protect a cell or subject from an organophosphate toxin. "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." See ***KSR v. Teleflex***, 550 U.S. ___, 127 S. Ct. 1727 (2007).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Radtke taken with Li and Davies, namely to intravenously administer a nucleic acid encoding PON1 to a subject exposed to an organophosphate toxin. One of ordinary skill in the art would have been motivated to combine the teaching to sufficiently deliver the nucleic acid to cells for expressing of PON1. See ***KSR v. Teleflex***.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments with respect to claims 1-5, 10-13, 19-25, 37-39 and 43 have been considered but are moot in view of the new ground(s) of rejection. As set forth in applicant's arguments filed on 11/17/06 (pages 9 and 14), at the time of filing, one of ordinary skill in the art would have had a reasonable expectation of success for practicing gene therapy.

Claims 1, 9, 14-16, 21, 36, and 40-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Radtke taken with Li and Davies as applied to claims 1-5, 10-13, 19-25, 37-39 and 43 above, and further in view of.

However, Radtke taken with Li and Davies taken with do not specifically teach using a polyadenylation (poly A) tail in the vector.

However, at the time the invention was made, one of ordinary skill in the art understands that poly A tail protects mRNA molecule from exonucleases and is important for transcription termination, for export of the mRNA from the nucleus and for translation. Scheffler teaches using poly A tail for regulating gene expression (column 5). In addition, tissue-specific, constitutive, and inducible promoters for expressing a gene of interest were well known to one of ordinary skill in the art as exemplified by Scheffler (column 6).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Radtke, Li, and Davies taken with Scheffler, namely to make and use a poly A tail in the vector in the method. One of ordinary skill in the art would have been motivated to combine the teaching for protecting the mRNA from exonucleases and for proper polyadenylation of the gene transcript.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Radtke, Li, and Davies taken with Scheffler, namely to make and use a promoter selected from a constitutive promoter, an inducible promoter, or a tissue specific promoter in the vector in the method. One of ordinary skill in the art would have been motivated to combine the teaching for properly or efficiently expressing the DNA encoding PON1 in a desired cell.

In view of the teaching of Radtke, Li, and Scheffler, one of ordinary skill in the art would have had a reasonable expectation of success for practicing the method because the promoter were well known to one of ordinary skill in the art for expressing a heterologous nucleic acid in a cell.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments with respect to claims 1, 9, 14-16, 21, 36, and 40-42 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

Claims 17 and 18 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 6:30 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz, SPE – Art Unit 1635, can be reached at (571) 272-0763.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Brian Whiteman/
Primary Examiner, Art Unit 1635